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A Randomised Controlled Trial of Manualized Cognitive Remediation Therapy in Adult Obesity

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Abstract

Objective: Research has indicated that individuals with obesity have neurocognitive deficits, especially in cognitive flexibility that may in turn impact on their weight loss and maintenance. Consequently, we examined the efficacy of a manualised face-to-face cognitive remediation therapy for obesity (CRT-O) within a randomised controlled trial, in terms of improving cognitive flexibility, reducing binge eating behavior, improving quality of life and helping with weight loss. **Methods:** 80 adults with obesity (body mass index >30 kg/m^2), 70% binge eaters, received three weekly sessions of group Behavioural Weight Loss (BWL) and then were randomised to 8 sessions of individual CRT-O or to a no-treatment control group. **Results:** Mixed-effects model analyses revealed that the CRT-O group had a significant improvement in their cognitive flexibility at post-treatment and 3-month follow-up compared to the control group (Cohen's d = 0.96 to 2.1). 68% of those in the CRT-O group achieved a weight loss of 5% or more at follow-up compared to only 15% of the controls (Cohen's d = 1.3). Changes in set-shifting predicted changes in weight ($p < .05$). Binge eating reduced in the CRT-O group compared to the control (Cohen's d = 0.80). **Discussion:** This is the first study showing the efficacy of CRT-O for obesity. Future CRT-O studies with longer follow-ups and pairing it with longer BWL programs are needed.

Keywords

Cognitive remediation therapy, adult obesity, executive function, weight loss, health related quality of life, binge eating, cognitive flexibility

Introduction

It is well known that obesity is associated with serious medical consequences and poor health related quality of life (Henderson & Brownell, 2004; Shaw et al, 2005). Evidence has also indicated an association between obesity and neurocognitive deficits, especially in executive function, irrespective of the presence of binge eating and independent of co-morbid medical conditions such as diabetes, hypertension and cancer (Gunstad et al., 2010; Smith et al., 2011), which are themselves associated with adverse cognitive effects (Luchsinger, 2012; Biessels, 2008; Reitz et al., 2007, Saykin et al., 2013). Executive function encompasses a diverse, overlapping group of higher-level neurocognitive processes such as decision making, response inhibition, organizational and planning abilities and cognitive flexibility that enable an individual to perform self-organised and goal-directed behaviours (Robbins, 1998). The mechanisms by which obesity is associated with executive deficits are however unclear. Some explanations include vascular pathology, inflammatory processes, neuroendocrine dysregulation, dopamine pathway dysregulation, alterations in levels of brain-derived neurotrophic factor and leptin biomarkers that impact the brain (Ylikoski et al., 2000; Rahmouni, 2005; Convit, 2003; Teunissen, 2003; Colcombe, 2003; Bjorntorp & Rosmond, 2000; Sapolsky, 1999). Each of these mechanisms, in isolation or combination, may contribute to the cognitive deficits in obesity.

Many obesity related eating behaviours rely heavily on neurocognitive processes and contribute to lapses in diet adherence (Houben et al., 2014; Price et al., 2016). For example, studies have found inefficient cognitive flexibility in set-shifting tasks in obesity (Wu et al., 2014; Perpiñá et al., 2016). This may help explain the enduring unhealthy eating behaviours in obesity, for example being ‘stuck’ in a disordered eating pattern and an inability to look at their situation from an alternate mindset. Deficits in cognitive flexibility, therefore, may be considered to be an important component of

obesity maintenance as well as being an impediment to patients benefiting and completing behavioural treatments for obesity in the long-term. Consequently, there is perhaps a bidirectional relationship between obesity and executive function, with obesity impacting on executive functioning via biological mechanisms and impaired executive functioning increasing the risk of obesity via disordered eating patterns and behaviours (Elias et al., 2003; Bruce-Keller et al., 2009; Smith et al., 2011; Stanek & Gunstad, 2013).

There is evidence that cognitive training programmes improve the targeted outcome and the therapeutic gains may also generalise to novel tasks in older adults (Ball et al., 2002; Willis et al., 2006; Anguera et al., 2013). Emerging evidence indicates that training specific cognitive components (e.g., working memory, inhibitory control, set- shifting) may be especially useful in the context of improving health behaviour (Tchanturia et al., 2015). For example, a study has shown that working memory training has been associated with a reduction in alcohol consumption in problem drinkers (Houben et al., 2011) and inhibitory control training has been shown to reduce chocolate consumption among chocolate lovers (Houben and Jansen, 2011).

A small trial (n=44) testing computerised executive function training with games in children with obesity found moderate effect sizes (standardised mean differences between 0.5 and 0.6) in executive function outcomes, such as improvements in a behaviour rating inventory of executive function and in a working memory task that favoured training (Verbeken et al., 2013), and also more capable at maintaining weight loss until 8 weeks post-training. Hence remediation of executive deficits may be vital to address behaviours related to weight loss and maintenance, yet neuropsychological processes and thinking styles are not addressed in current treatments (James & Linton, 2009). To our knowledge the efficacy of this approach has not yet been investigated in adults with obesity.

Cognitive Remediation Therapy for Obesity (CRT-O)

Cognitive remediation therapy (CRT), an intervention originally formulated to improve functioning in schizophrenia (Eack et al., 2015; Wykes et al., 2011), is also commonly used to treat people with addiction (e.g., Rupp et al., 2012) and eating disorders (Tchanturia et al., 2014). CRT addresses the processes of thought, rather than the content (Tchanturia et al., 2014, 2015). For the purposes of this study, we adopted CRT for anorexia nervosa and developed CRT-Obesity (CRT-O), which was designed to provide individuals with the tools to think differently. CRT-O's aim was twofold: 1) To enhance cognitive flexibility and 2) to aid weight loss and prevent further weight gain by linking the thinking style to dietary and physical activity, but not addressing diet or physical activity directly. In this study, CRT-O was administered as a brief eight-session 45-minute individual face-to-face therapy; it was not done via a computer. Simple cognitive tasks and exercises were administered that encouraged reflective learning and insight into a participant's own thinking process together with intra-session experimentation.

A psychological model on obesity maintenance (COMM: Raman et al., 2013) has argued that psychological variables, including mood and binge eating behaviour, interact with executive functioning and impact on obesity. Obesity has been shown to increase the risk of developing depression and depression has been found to be predictive of obesity (Luppino et al. 2010) and there is a dose–response gradient in that the association between depression and obesity was stronger than the association between depression and being overweight (Renn et al., 2011). There is ample evidence that depressive disorders are also associated with deficits in attentional function, executive control and lowered cognitive flexibility (Davis & Nolen Hoeksema, 2000) verbal learning and memory (Watkins & Teasdale, 2001) and interpretation biases [Disner et al.2011; Marrazziti et al., 2010; Ukjermann et al., 2008; Peron et al., 2011). Furthermore, there is evidence that individuals who binge-eat may have more difficulty

losing weight (e.g., Texeira et al., 2004). Several studies have reported an increased stop signal reaction time (an index of response inhibition), as well as greater inhibitory deficits related to exposure to food stimuli in individuals with binge eating compared to weight matched controls who do not binge eat (Svaldi et al., 2010). Given that loss of control appears to be a central feature of BED, it is not surprising that individuals with BED often display elevated rates of impulsivity and difficulty maintaining goal-directed behavior (Colles et al., 2008).

The aim of this study was to test the efficacy of the novel manualized CRT-O. In this study, all participants received a brief group-based Behaviour Weight Loss Treatment (BWLT) and were then randomised to a CRT-O group or a no-treatment control group. BWLT addressed health literacy and weight-loss strategies including psycho-education, weight monitoring, dietary advice and exercise planning. Perceived barriers to weight management were discussed and challenged in BWLT. The CRT-O training targeted executive function deficits and changes in thinking style, in particular cognitive flexibility and task switching.

The primary hypothesis was that participants who received BWLT plus CRT-O would demonstrate improved cognitive flexibility at post treatment and at 3-month follow-up, compared to those who received BWLT only. The secondary hypotheses were that, compared to those who received BWLT only, participants who received BWLT plus CRT-O would demonstrate improved (i) weight loss (assessed by percentage weight lost across time points) (ii) better Health related quality of life (HRQoL), (iii) improved depression symptoms and (iv) reduced binge eating at post treatment and 3-month follow-up. The third hypothesis examined whether changes in cognitive flexibility predicted weight changes.

Methods/Design

Participants

Eighty individuals with obesity were recruited via direct advertisement to the community in Sydney, Australia. Inclusion criteria were: BMI ≥30 kg/m2, age 18 to 55 years, current weight under 180 kg, ability to provide informed consent and having completed 10 years of education in English. Participants were recruited from 15th January 2013 to 25th March 2014. Attention was drawn to the recruitment through the general and social media. Participants received 20 Australian dollars to attend the baseline and follow-up assessments for each visit as financial compensation for their participation in the study. Participants were excluded if they had a history of psychosis, head injury, neurological disorder including degenerative or inflammatory conditions or stroke, diagnosed attention deficit hyperactivity disorder, epilepsy, developmental or intellectual disability; were unable to complete the testing (e.g. due to hearing, vision or language impediment); were on regular sedative or stimulant medication; and/or report regular substance use or abuse (for alcohol, more than four standard drinks five times a week). The sample size was determined based on power estimates using Cohen's tables for an estimated medium effect size of 0.6, power of 0.8, one-tailed test, P <0.05 and attrition of 20%. The effect size of 0.6 was considered by the pilot data we conducted, and on the effect size of CRT trials on anorexia nervosa. One tailed was chosen because we expected the difference to be only in one direction, as we did not expect any changes in executive function in the control group. Although there were no previous studies of adults with obesity, these levels were commensurate with those achieved by a study to enhance self-regulatory abilities for weight-control in children with obesity (Verbeken et al. 2013).

Procedure

Recruitment was via advertisements placed on social media sites, university and

community center notice boards and via media interviews with journalists from metropolitan and community newspapers. The initial screen was by phone to establish potential eligibility. This was followed by a face-to-face psychological and neuropsychological assessment (described below). All 80 participants then received group-based BWLT that ran once a week for 3 weeks, each session lasting 90 minutes. At the completion of the third and final session, participants were randomly allocated to CRT-O or no treatment. Individuals in the no-treatment control were instructed to continue their weight loss efforts, but were not instructed how to do this. Randomisation and allocation concealment were conducted using an online randomizer. A flow chart of the procedure can be found in Figure 1. The procedure was approved by the ethics committee of the local university (UWS HREC approval H9787). The trial is registered with the Australian New Zealand Registry of Clinical Trials (Trial ID ACTRN12613000537752). The protocol section of this study has been published (Raman et al., 2014).

Assessment

All assessment measures were administered at baseline. The BWLT commenced within 2 weeks of baseline assessment and was followed immediately by CRT-O (3 weeks of BWLT and 4 to 6 weeks of either CRT-O or no treatment). Hence participants completed their end of treatment assessment 9-11 weeks after baseline testing, and again at the 3-month post-CRT follow-up (Please see Fig 1. for subject flow through enrollment and follow-up).

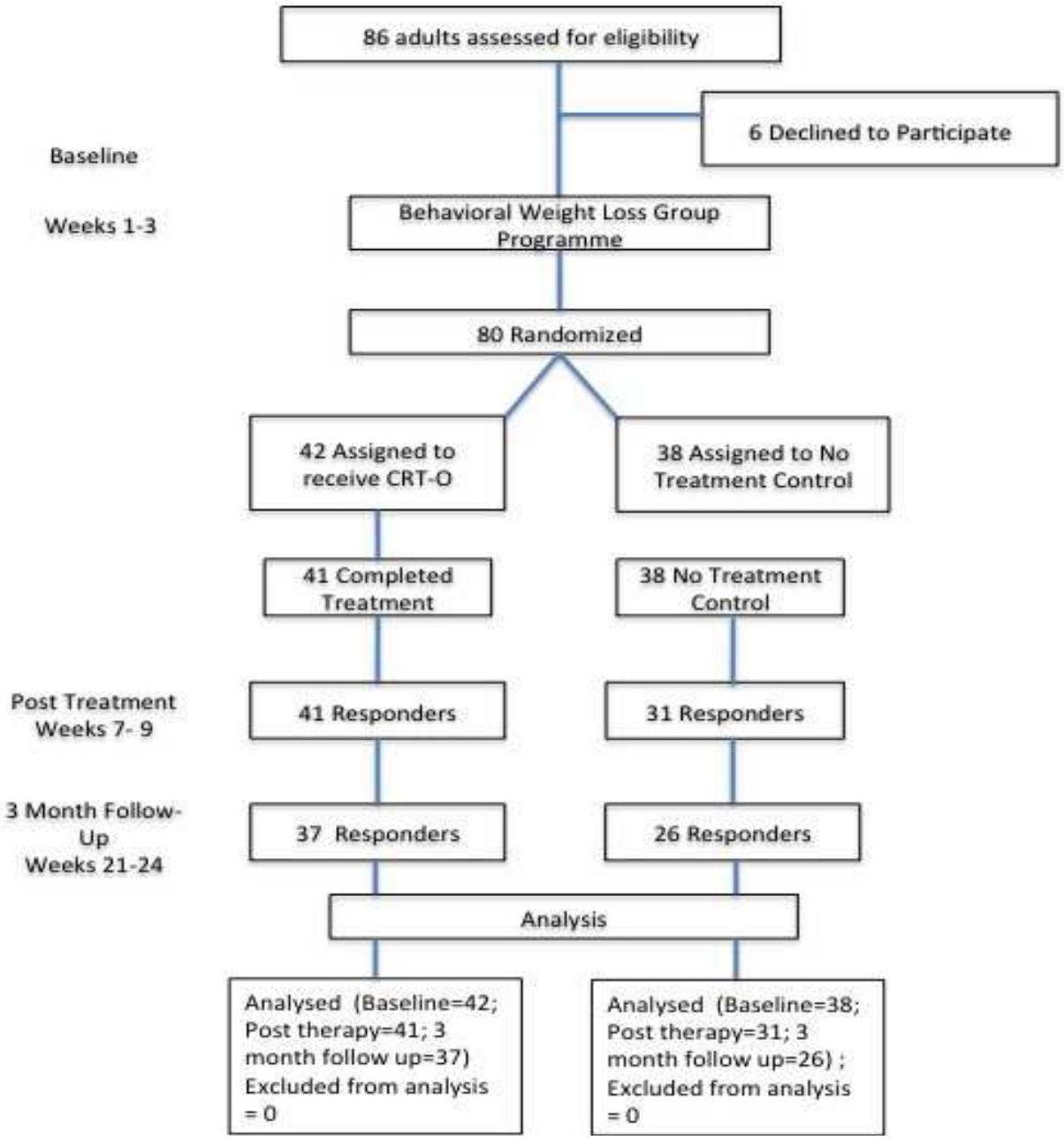
Weight and body mass index

For participants, we measured height and weight (kilograms) with calibrated scales, from which we derived body mass index (BMI) in kg/m^2.

Demographics and medical history

Age, gender and education were recorded in the general questionnaire. This form also included medical history, current medical conditions and medication.

Fig 1. Participant Flow Diagram



Neuropsychological assessment

The two neuropsychological tests employed were selected because they covered the cognitive flexibility aspect of executive functioning, which was confirmed by our unpublished meta-analysis to be the area most affected in individuals with obesity. The tests were administered individually to all participants by a trained clinical psychologist.

1. The Wisconsin Card Sorting Test (WCST) 64: The computerised version of WCST (Grant, 1951; Harris, 1990; Heaton, 1981) was used. The WCST measures categorisation, inference, testing of hypotheses, cognitive flexibility, cognitive inhibition and response to feedback (Mobbs et al., 2010). The number of perseverative errors was the dependent measure. The WCST is considered to be a valid measure of abstract reasoning ability to maintain an appropriate planning and problem-solving strategy across changing stimulus conditions to achieve a future goal, and it is the most widely used test of executive function (Lezak et al. 2012).

2. Trail Making Test (TMT) (Battery, 1944): The TMT was used to assess psychomotor speed, visual integration, cognitive flexibility and inhibitory control. This test measures the participant's ability to connect written numbers in an ascending order (Trail A) and afterwards, to connect numbers and letters, alternating numbers in ascending order and letters in alphabetical order (Trail B), for example, 1-A- 2-B (Lezak et al. 2012). For this study, the derived score (TMTB-TMA) was used as an outcome variable to control for speed of processing.

Psychological self-report measures

Depression, Anxiety and Stress Scales

Depression symptoms in this study were measured by the Depression, Anxiety and Stress (DASS) Scales (Henry & Crawford, 2005). This test has been validated in a number of clinical and non-clinical populations and has been shown to be psychometrically sound with good reliability and validity to measure depressive symptoms in the previous week (Henry & Crawford, 2005; Antony et al. 1998). A Score over 10 suggests some mild symptoms of depression, whereas a score over 28 suggests extremely severe symptoms of depression.

Binge eating

Binge eating was first measured by the Eating Disorder Examination Questionnaire (EDEQ: Fairburn, 2008), and then assessed via a clinical interview, by a clinical psychologist. Responses to the question on the number of binge eating episodes per week were clarified via the clinical interview to ascertain the clinical definition of a binge eating episode as per the DSM 5 criterion. Any discrepancies between the EDEQ and the clinical interview, the clinical interview took precedence.

Health-related quality of life

HRQoL was measured with the 12-item Short Form (Ware et al., 1996), which is a widely used quality of life measure with good construct and criterion validity and with adequate sensitivity to change. Mental health related quality of life is measured by 1) how participants felt if they accomplished less than usual, 2) if they had trouble doing any work or activities as carefully as usual as a result of an emotional problem, and 3) as to how calm, peaceful, downhearted or blue they felt in the past 4 weeks.

Interventions

Behavioural Weight-Loss Group Intervention

The BWLT in this study targeted diet and exercise through behavioural modification

techniques over three 90-minute weekly sessions. In the first session, obesity-related risk awareness, challenges with perceived barriers and perceived personal control were discussed in depth. Cognitive challenging techniques were taught and in-session goal setting practices were conducted. In the second session, participants received comprehensive education about nutrition, hunger management and healthy eating practices. Problem-solving techniques were taught so that participants can effectively deal with difficult situations that threaten their weight-control efforts. National physical activity guidelines were discussed and further training given on goal setting and goal achievement. In the last session, attention was given to motivation enhancement and relapse prevention strategies to help individuals maintain their weight loss.

Cognitive Remediation Therapy for Obesity

CRT-O is a manualized intervention that consists of mental exercises aimed at improving cognitive strategies, thinking skills and information processing through practice. CRT promotes reflection on thinking styles, develops metacognition and helps to explore and apply new thinking strategies in everyday life. The primary function of CRT is to improve the thinking process rather than the content (Tchanturia, et al 2014, 2015). In the absence of a published manual for obesity, a CRT-O manual was developed to meet the needs of the participants with obesity for the purposes of this randomized controlled trial (RCT). The intervention was conducted face-to-face and delivered by the first author (JR), who is an endorsed clinical psychologist in Australia. The principles, structure and main components of the original CRT-AN were maintained (Tchanturia et al., 2010). Some important modifications, however, were made to adapt the manual for obesity. We replaced tasks that encouraged abstract, global thinking with tasks that facilitated attention to detail. A small pilot study had previously reported moderate to strong effect sizes in tasks measuring detailed focus in overweight participants (Roberts et al., 2007). We also added tasks that looked at problem solving skills. In the other tasks that we retained from the CRT-AN manual, reflective thinking

techniques were redirected to enhance organization, planning and problem solving in a focused fashion (Smith, Raman, Hay, 2015).

Data collection, management and analysis

Data were collected at baseline, end-of-treatment and the 3-month follow-up by the trial therapist. Data were entered and coded by a research assistant, blind to group allocation, and stored at a secure university facility according to university protocols.

T-tests were done using the Statistical Package for Social Sciences (SPSS: v22) to compare groups on baseline outcome variables, clinical and demographic data. Mixed-effects models (MEM) were used with SAS 9.2 (SAS Institute Inc., Cary, NC) to examine the association between the outcomes and the CRT-O treatment over time. We used mixed effects modeling because it accounts for longitudinal data sets with missing data and repeated measurements made at irregular time intervals (Littell et al., 2006).

The mixed-effects model consists of two parts: fixed effects and random effects. Fixed effects describe the population average of baseline and follow-ups, and random effects describe the participant-specific heterogeneity in those measures.

The model took the form:

$$Y_{it} = Intercept + \beta_1(Group) + \beta_2(Time1) + \beta_3(Time2) + \varepsilon_{it} + u$$

In this model, Y_{it} is the outcome of interest of the participant *i* at time *t*, the first three four terms in the right-side of equation are the usual fixed effect terms and ε_{it} represents the usual, normally distributed residual error. Group is for the treatment group (with control group taken as a reference group) and Time1 and Time 2 are for the post intervention and 3-month follow-up, respectively. Group, Time1 and Time2 are dummy variables. For a random effect, a random intercept, u_i is introduced accounting for the variance between participants at baseline (analyses of the random effect can be found in Appendix A). The analyses were done twice, first without using any covariates and then including as covariates any baseline outcomes that were statistically significant.

Effect sizes between and within the two groups were calculated using Cohen's d computed with the pooled standard deviation. For transparency, a series of univariate analyses were conducted to corroborrate the MEM analyses, and these were reported in a footnote next to the corresponding MEM analysis.

Results

Baseline results

Our participant pool comprised of 86% females. 67% participants were employed outside the home, majority fulltime, 7% were engaged in home duties and the remainder were unemployed, studying or seeking employment. The treatment group was higher in the number of years of education ($p < .05$). Baseline outcome measures did not show any significant difference between groups except for the depression scores, which was higher in the treatment group ($p<.05$). Baseline demographics and clinical characteristics of the participants are shown in Table 1. There were no differences at baseline between people who dropped out at follow-up and people who did not drop out in terms of weight ($p = 0.67$) and WSCT perseverative responses ($p = 0.776$), or any other baseline measures ($p > 0.05$)

Table 1. Means (standard deviation) of baseline demographic and clinical characteristics: age, education in years, WCST perseverative errors, TMT derived scores, BMI, depression, mental health related quality of life and binge eating frequency for CRT-O and control groups.

	Control Group n=38 Mean (SD)	Treatment Group n=42 Mean (SD)	Sig (df=78) t,p
Years of education	13.5 (2.3)	15.0 (2.4)	t = 2.8; p = 0.006
Age	42.2 (8.8)	40.6 (7.0)	t= -0.92; p=0.36
WCST Persev Errors	9.0 (5.8)	10.7 (5.0)	t=1.50; p=0.14
TMT Derived	34.4 (26.9)	34.7 (35.1)	t=0.03;p=0.98
BMI (kg/m^2)	39.2 (7.4)	40.3 (7.8)	t=0.68; p=0.51
Depression	13.3 (12.2)	19.1 (11.2)	t=2.21; p=0.03
Mental Health related QoL	45.7 (9.4)	46.9 (8.4)	t=0.62; p=0.54
Binge Eating Frequency	9.3 (10.6)	9.3 (8.7)	t=0.01; p=0.99

NOTE: WCST: Wisconsin Card Sorting Task; TMT derived (Trail B-Trail A was calculated to control for speed of processing)= Trail making test; BMI = body mass index

Primary outcome: cognitive flexibility

Table 2 reports means and standard deviations of WCST and TMT derived. Table 3.1 report fixed effect estimates of model parameters, when adjusted by time and including random intercept, along with their standard error and the result for the test of their significance (random effects can be found in Appendix A). The treatment group (Group) shows negative association with both of WCST preservative errors and TMT derived score. This means that treatment group reports significantly lesser mean WCST preservative error and TMT derived score compared to control group adjusted for the effect of time (β = -1.82, p = <.05 for WCST errors and β = - 11.74, p = <.05 for TMT derived score)[1]. Including baseline depression scores or education in the model did not significantly change the results.

The effect size of the changes in the WCST from baseline to three-month follow-up in the CRT-O group was Cohen's d of 1.7, whereas the effect size of the changes in the WCST from baseline to 3-month follow-up in the control group was Cohen's d of -0.1. Similarly, the effect size of the changes in the TMT B-A in the CRT-O group was Cohen's d of 0.78, whereas the effect size of the changes in the TMT B-A in the control group was Cohen's d of -0.05.

Table 2. Means (standard deviation) of the executive function tests, weight change in percentage, BMI, depression, quality of life and frequency of binge eating outcomes at baseline, post-treatment and three-month follow-up, for CRT-O and control groups

[1] Two linear univariate analyses were conducted to corroborrate the MEM results. The dependent variable was WCST perseverative errors at 3 month follow up, the independent variable was group, and the covariate was the WCST perseverative errors at baseline: F = 35.7; p < 0.001, partial eta squared .34. This suggests that the CRTO group had a significantly lower score of the WCST at 3-month follow-up compared to the control group, when controlling for baseline data, replicating the MEM analyses. When the dependent variable was changed to TMT B-A, similar results were found.

	Treatment			Control		
	Baseline n = 42 M(SD)	Post n=41 M(SD)	3MFU n=37 M(SD)	Baseline n = 38 M(SD)	Post n=31 M(SD)	3MFU n=26 M(SD)
WCST Persev Errors	10.7 (5.0)	5.0 (1.8)	4.5 (0.9)	9.0 (5.8)	8.2 (4.7)	9.6 (5.6)
TMT B-A	34.7 (35.1)	14.9 (7.2)	15.0 (5.9)	34.4 (26.9)	33.6 (24.5)	35.9 (26.1)
Weight change (percent)	-	0.04 (0.03) (from baseline to Post)	6.6 (4.0) (from baseline to 3MFU)		-0.02 (0.04) from baseline to post)	-1.2 (7.5) (from baseline to 3MFU)
Weight	111.7 (21.5)	108.1 (21.3)	105.5 (20.7)	108.1 (18.7)	111.3 (20.7)	109.3 (18.9)
BMI	40.3 (7.7)	38.9 (7.6)	38.3 (7.6)	39.2 (7.4)	39.7 (8.4)	38.8 (8.4)
Depression	19.1 (11.2)	4.5 (5.1)	5.8 (8.6)	13.3 (12.2)	15.4 (12.2)	11.9 (12.1)
Mental health related Quality of Life	47.0 (8.4)	53.1 (7.6)	50.5 (10.7)	45.7 (9.4)	45.2 (13.4)	48.3 (12.0)
Binge eating	9.3 (8.7)	3.2 (5.7)	3.4 (6.0)	9.3 (10.6)	11.6 (11.9)	9.2 (10.6)

Note: 3MFU = three month follow-up; Post = post-treatment; WCST Persev errors = Wisconsin Card Sorting Test perseverative errors; TMTB-A= Trail B minus Trail A Derived; BMI = body mass index

Table 3.1: Fixed effect model estimates for primary outcomes, WCST and TMT (the control condition is coded as 0 and the treatment condition is coded as 1)

Primary Outcomes	Effect	Estimate	SE	P-Value
WCST	Intercept	10.84	0.67	<0.001
	CRT-O Group	-1.82	0.84	0.030
	Time2	-3.06	0.59	<0.001
	Time1	-3.43	0.56	<0.001
TMT	Intercept	40.63	3.39	<0.001
	CRT-O Group	-11.74	3.94	0.004
	Time2	-10.17	3.63	0.010
	Time1	-11.06	3.45	0.002

CRT-O group = condition effect adjusting for effect of time

Time1 (at post intervention) and time 2 (at 3-month follow-up) = effect of outcome at each Time.

Secondary outcomes: weight change, binge eating, BMI, depression and quality of life

Weight change

Weight change defined as the difference (percentage reduction) in weight between weight at baseline period and at time 1 (post treatment), and time 2 (3 month follow up). Table 3.2 reports fixed effect estimates of model parameters along with their standard error and the result for the test of their significance. The treatment group (CRT-O Group) shows positive association with weight change percentage. This means that treatment group reports significantly higher weight change percentage compared to control group adjusted for the effect of time ($\beta = 2.27$; $p < .0001$), but only for Time 2 ($\beta = -3.2$; $p < .0001$)[2]. There were no significant differences in weight change percentage between the two groups at Time1 (post treatment). Controlling for baseline depression scores or

[2] A linear univariate analysis was conducted to corroborrate the MEM results. The dependent variable was weight at 3 month follow up, the independent variable was group, and the covariate was the weight at baseline: $F = 21.7$; $p < 0.001$, partial eta squared .27, replicating the MEM analyses.

education did not change the results.

As can be seen in Table 2, at 3-month follow-up (Time 2), participants who completed CRT-O had lost on average 6.6% of weight (95% CI 5.6 to 9.1), whilst controls gained 1.2% of weight (95% CI -4.6 to 2.5). The effect size for this difference between groups was large, with a Cohen's d of 1.3. In addition, 68% of those in the CRT-O group achieved a weight loss of 5% or more, compared to only 15% of the controls.

Table 3.2. Mixed Effect Model estimates for weight change percentage. (The control condition is coded as 0 and the treatment condition is coded as 1)

Outcome	Effect	Estimate	SE	P-Value
Weight change percentage	Intercept	-1.19	0.47	0.010
	CRT-O Group	2.27	0.48	<0.001
	Time2	3.21	0.59	<0.001
	Time1	-0.009	0.57	0.880

Binge eating, BMI, depression and quality of life

As shown in Table 3.3, when adjusted by time and including random intercept, the treatment effect is statistically significant for binge eating frequency and mental health quality of life, which suggests that the treatment improves these outcomes. However, for mental health quality of life, this was only significant at Time 1. As shown in Table 3.3, when adjusted by time and including random intercept, the treatment effect was not significant for BMI or depression.

Table 2 shows that individuals in the CRT-O group were on average binge eating around 9.3 (SD: 8.7) times a month at baseline, but at the end of treatment and at three month follow-up this had reduced to an average of 3.3 (SD: 5.8) times a month (Cohen's d = 0.8). In contrast, the control condition was binge eating 9.3 (SD: 10.6) times a month on average at baseline, and 9.2 (SD: 10.6) times a month at 3-month follow-up (Cohen's d = 0.0).

Table 2 shows that individuals in the CRT-O group's mental health quality of life scored 46.9 (SD: 8.35) at baseline, and it increased to an average of 53.1(SD: 10.5) at post-treatment (Cohen's d = 0.65). In contrast, the control condition had an average score on the mental health quality of life of 45.7 (SD: 9.4) at baseline, and 45.2 (SD: 13.4) at post-treatment (Cohen's d = -0.04).

Table 3.3: Mixed Effect Model estimates for BMI, depression, binge eating and mental health quality of life. (The control condition is coded as 0 and the treatment condition is coded as 1)

Secondary Outcomes	Effect	Estimate	SE	P-Value
BMI	Intercept	39.92	1.24	<0.001
	CRT-O Group	-0.31	1.70	0.860
	Time2	-1.42	0.27	<0.001
	Time1	-0.56	0.26	0.030
Binge eating frequency	Intercept	12.09	1.48	<0.001
	CRT-O Group	-4.91	1.82	0.010
	Time2	-3.42	1.10	0.002
	Time1	-2.76	1.06	0.010
Depression	Intercept	17.74	1.66	<0.001
	CRT-O Group	-2.63	2.09	0.230
	Time2	-7.92	1.34	<0.001
	Time1	-7.18	2.35	<0.001
Mental health related quality of life	Intercept	44.46	1.50	<0.001
	CRT-O Group	3.74	1.84	0.040
	Time2	2.28	1.53	0.140
	Time1	2.92	1.40	0.040

Note: WCST- Wisconsin Card Sorting Task; TMT- Trail Making Task; BMI- Body Mass Index

Change of cognitive flexibility predicted changes in weight

For the outcome weight change in percentage, the effect of the treatment is assessed after adjusting for WCST perseverative errors and TMT derived score in addition to time. Estimated model parameters coefficients are shown in Table 3.4. Treatment effect remains significant ($p < .05$). WCST perseverative error was statistically significant, but TMT score was not.

Table 3.4: **Estimates of Effects of Time, Condition, and Change of cognitive flexibility on Weight Change Percentage**

Effect	Estimate	SE	p
Intercept	0.85	0.82	0.300
CRT-O Group	1.87	0.50	<0.001
Time2	2.62	0.62	<0.001
Time 1	-0.74	0.60	0.220
WCST	-0.15	0.05	0.010
TMT	-0.01	0.01	0.290

WCST: Changes in Wisconsin Card Sorting Test; TMT: Trail Making Test.

Discussion

This is the first study to evaluate the efficacy of manualised, face-to-face cognitive remediation therapy for adult obesity. Results of this study indicated that CRT-O was efficacious at improving cognitive flexibility compared to the control group at post-treatment, and this improvement was maintained at the 3-month follow-up. Results also showed that individuals in the CRT-O group lost significantly more weight at the 3-month follow-up (6.6% weight loss), measured by weight change percentage across the two points, and that changes in cognitive flexibility, as measured by the WCST, predicted changes in weight. Furthermore, the CRT-O group significantly reduced participants' binge eating frequency from pre to post treatment, and this was maintained at follow-up. It also improved the mental health quality of life from pre to post-treatment, but this was not maintained at three-month follow-up. These improvements were achieved after only completing eight, twice weekly, 45-minute CRT-O sessions.

Consistent with previous studies of CRT in anorexia nervosa (e.g., Tchanturia et al., 2014), our results also showed that individuals improved in cognitive flexibility after

CRT-O. Results from our study support the explanation that the initial executive improvements may predict weight loss outcomes i.e., improvement in cognitive flexibility may have enabled the participants to engage in better lifestyle choices that in turn resulted in subsequent weight loss. However, only WCST predicted weight change. The other measure of cognitive flexibility, TMT, which is specifically a measure of task switching, did not predict changes in weight. The correlation between WCST and TMT (B-A) has been shown to be around 0.3 (Chaytor, Schmitter-Edgecombe, Burr, 2006), suggesting that they are not different measures of the same construct (cognitive flexibility), but that they are measuring non-overlapping variance. WCST is the most widely used measure of cognitive flexibility. While the participants' cognitive flexibility may have improved as a result of CRT-O, the executive improvements that were maintained at the three-month follow-up may relate to improvements in participants' weight loss and related behaviours. For example, a meta-analysis of twelve studies found an improvement in memory and attention performances with weight loss in individuals with obesity (Siervo et al., 2011). Recent findings in bariatric surgery patients, have suggested that weight loss might be linked to improved cognitive function (e.g., Alosco et.al., 2014).

A noteworthy finding is the changes in binge eating in the treatment group. Around 70 % of our participants, met criteria for binge eating disorder (BED). Although the findings from empirical literature are mixed about the independent contribution of a BED diagnosis in obesity to neurocognitive deficits (Davis et al., 2010, Duchesne et al., 2010; Svaldi et al., 2014; Svaldi et al., 2010), given that loss of control in eating appears to be a central feature of BED (Colles et al., 2008), it is not surprising that individuals with the disorder often display elevated rates of impulsivity and reduced executive function (Grucza et al., 2007; Manwaring et al., 2011; Svaldi et al., 2012; Wu et al., 2013). Results from our study demonstrated a Cohen's d effect size of 0.8 on change of binge eating frequency. This is comparable to the effect size of five pooled psychological

studies comprising of 197 participants that resulted in a Cohen's d of 0.8 as shown in a meta-analysis (Vocks et al., 2010). The psychological studies in this meta-analysis comprised of an average of 20 sessions of cognitive behavioural therapy (Vocks, et al., 2010), suggesting that eight 45-minute sessions of CRT-O might be an alternative treatment for BED.

Our study found that those in the CRT group had improvements in mental health QoL, but only at post-treatment. This suggests that face-to-face intervention and not weight loss was responsible for these results. In fact, weight loss did not lead to a significant improvement in mental health QoL, contradicting the majority of studies showing improvements in QoL after weight loss achievement (Fontaine and Barofsky, 2001; Blissmer et al., 2006; Kolotkin et al., 2009).

This study did not find that CRT-O had an effect on participants' depression at post therapy assessment or three-month follow-up. These results are consistent with the results of a previous study on computer-assisted cognitive remediation therapy in patients with a major depressive disorder (Elgamal et al., 2007). In Elgamal's et al (2007) study, patients who received cognitive training improved on a range of neuropsychological tests, but results did not show any change in depressive symptom scores.

In order to understand the magnitude of these findings, it is important to compare these results with data from previous weight loss trials. A meta-analysis of 80 behavioural weight loss studies established a mean weight loss of 5 to 8.5 kg (5% to 9% of body weight) within 6 months, with most providing 24 weekly sessions (Franz et al., 2007). Weight loss was shown to plateau at approximately 6 months in this meta-analysis, with study participants experiencing weight regain at the two-year follow-up. The current study's CRT-O produced comparable results 5 months after baseline (3 month follow-up). A 5-10% reduction in total body weight can produce significant health benefits (e.g., lower blood pressure, lower glucose levels, and improved lipid

profiles). Since weight loss for the purpose of improving health status is recommended for individuals with obesity, achieving and maintaining a 5-10% weight loss should be considered a meaningful accomplishment (Wing & Hill, 2001). Although CRT-O was not a weight loss intervention per se, it was able to have an effect on weight that was clinically significant. In this study, 68% of those in the CRT-O group achieved a weight loss of 5% or more at follow-up compared to only 15% of the controls. Based on the results of this study, cognitive remediation therapy could be a nice adjunct to behavioural weight loss programmes. Interestingly, although this study found a significant weight loss (> 5%) in 68% of participants in the CRT-O group, no differences between groups in BMI were found. It is important to highlight that BMI is an estimate of body fat, whereas weight change percentage is the most widely used outcome measure, as documented by Franz et al (2007) in their meta-analysis of 80 behavioural weight loss studies. Weight loss success is commonly defined as 5% weight loss, not BMI change (Wing & Hill, 2001).

One limitation of this study includes lack of blinding of participants and assessor. However, using an objective, computerized, neuropsychological test of set shifting, a key feature in executive function (WCST) as one of the main outcome variables mitigated the experimenter effect (i.e., response bias) to an extent. Another limitation of this study was the lack of an active treatment arm controlling for non-specific therapeutic effects. Although promising, the treatment group did receive more treatment than the control group and it is possible that this could have enhanced the effects of CRT-O. It is also possible that the effect of CRT-O is a placebo effect (e.g. participants get better because they are seeing someone for their weight). However, other treatments, such as weekly support using motivational interviewing, do not impact on weight to the same extent as CRT-O (Barnes & Ivezaj, 2015), so unlikely to be a placebo effect. Importantly, this trial needs to be replicated and CRT-O should be compared to a behavioural weight loss program. We expect that by combining these two programmes weight loss might be

maintained long term, compared to behavioural weight loss alone. However, our control group provided a great comparison to a real world scenario, and highlights the importance of treatment.

Another limitation is that this study had a relatively short follow-up period of three months. Hence, the follow-up period in this study was too short to make definitive conclusions about weight regain in either condition. Studies with longer follow-ups are needed to make more definitive conclusions about treatment effects in either condition. A further limitation was that although our CRT-O intervention included planning exercises, we did not test planning in our participants, before and after CRT-O. Future research should include Tower of London (Donders & Larsen, 2012) or other planning related tests to examine whether planning efficacy is impacted after the CRT-O intervention.

This study also had some strengths. These include the use of a randomized controlled study design and a novel manualized cognitive remediation treatment for obesity. Another strength was that it presents outcomes on a community sample and therefore is representative of a non-clinical, wider community.

Conclusion

The findings of this study suggest that brief CRT-O (eight 45-minute sessions) is an efficacious treatment to enhance weight loss, improve cognitive flexibility and reduce binge eating behaviour in individuals with obesity. The ease of delivery of the CRT-O program suggests that it could be incorporated as an adjunctive therapy along with BWLT and/or other weight management programmes. CRT-O should now be compared to an active treatment, and long-term follow-ups must be evaluated.

References

Abbate-Daga, G., Buzzichelli, S., Marzola, E., Amianto, F., & Fassino, S. (2012). Effectiveness of cognitive remediation therapy (CRT) in anorexia nervosa: A case series. Journal of Clinical and Experi-mental Neuropsychology, 34, 1009–1015. doi: 10.1080/13803395.2012.704900

Alosco, M. L., Galioto, R., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., … Gunstad, J. (2014). Cognitive Function Following Bariatric Surgery: Evidence for Improvement 3 Years Post-Surgery. *American Journal of Surgery, 207*(6), 870–876. http://doi.org/10.1016/j.amjsurg.2013.05.018

Anguera, J. A., Boccanfuso, J., Rintoul, J. L., Al-Hashimi, O., Faraji, F., Janowich, J., … Gazzaley, A. (2013).Video game training enhances cognitive control in older adults. Nature, 501(7465), 97–101.

Antony, M. M., Bieling, P. J., Cox, B. J., Enns, M. W., & Swinson, R. P.(1998). Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales (DASS) in clinical groups and a community sample. Psychological Assessment, 10(2), 176-181.

Aronne, L. J., Wadden, T., Isoldi, K. K., & Woodworth, K. A. (2009). When prevention fails: Obesity treatment strategies. American Journal of Medicine, 122, 4 (1), S24-32. .

Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., … Willis, S. L. (2002). Effects of cognitive training interventions with older adults: a randomized controlled trial. Journal of American Medical Association, 288(18), 2271–2281.

Battery, A.I.T. (1944). The Trail Making Task: Manual of Directions and Scoring. Washington, DC. Retrieved from http://www.biomedcentral.com/1471-2377/7/10

Best, J. R., Nagamatsu, L. S., & Liu-Ambrose, T. (2014). Frontiers in Human Neuroscience. 8, 353.

Biessels, G. J., Deary, I. J., Ryan, C. M. (2008). Cognition and diabetes: a lifespan perspective.
The Lancet Neurology, 7(2), 184–190.

Bjorntorp, P., & Rosmond, R. (2000). Neuroendocrine abnormalities in visceral obesity. International Journal of Obesity and Related Metabolic Disorders, (suppl 2), S80–S85.

Blaine, B. (2008). Does depression cause obesity?: A meta-analysis of longitudinal studies of depression and weight control. Journal of Health Psychology, 13(8), 1190-1197.

Blissmer, B., Riebe, D., Dye, G., Ruggiero, L., Greene, G., & Caldwell, M. (2006) Health- related quality of life following a clinical weight loss intervention among overweight and obese adults: Intervention and 24 month follow-up effects. Health and Quality of Life Outcomes, 4, 43.

Brinkworth, G. D., Buckley, J. D., Noakes, M., Clifton, P. M., & Wilson, C. J. (2009) Long- term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. Archives of International Medicine, 169(20), 1873-1880.

Brogan, A., Hevey, D., & Pignatti, R. (2010). Anorexia, bulimia, and obesity: shared decision making deficits on the Iowa Gambling Task (IGT). Journal of International Neuropsychological Society, 16(4), 711-715.

Brownell, K. D. (2010). The humbling experience of treating obesity: Should we persist or desist? Behaviour Research and Therapy. 48(8), 717–719.

Bruce-Keller, A. J., Keller, J. N., Morrison, C. D. (2009). Obesity and vulnerability of the CNS. Biochimica et Biophysica Acta, 1792(5), 395–400.

Busch, A. M., Whited, M. C., Appelhans, B. M., Schneider, K. K., Waring, M. E., DeBiasse,
M. A., … Pagoto, S. L. (2013). Reliable change in depression during behavioral weight loss treatment among women with major depression. Obesity, 21(3), 211.

Colcombe, S., & Kramer, A. (2003) Fitness effects on the cognitive function of older adults: A meta-analytic study. Psychological Science, 14(2), 125-130.

Colles, S. L., Dixon, L. B., & O'Brien, P. E. (2008). Loss of control is central to psychological disturbance associated with binge eating disorder. Obesity, 16(3), 608–614.

Convit, A., Wolf, O. T., Tarshish, C., & de Leon, M. J. (2003). Reduced glucose tolerance is associated with poor memory performance and hippocampal atrophy among normal elderly. Proceedings of the National Academy of Science of the USA, 100(4), 2019– 2022.

Dalle Grave, R., Calugi, S., Petroni, M. L., Di Domizio, S., Marchesini, G. & QUOVADIS Study Group. (2010). Weight management, psychological distress and binge eating in obesity: A reappraisal of the problem. Appetite, 54(2), 269–273.

Danner, U. N., Ouwehand, C., van Haastert, N. L., Hornsveld, H., de Ridder, D. T. (2012).
Decision-making impairments in women with binge eating disorder in comparison with obese and normal weight women. European Eating Disorders Review. 2(1), e56-e62.

Davis, C., Patte, K., Curtis, C., & Reid, C. (2010). Immediate pleasures and future consequences. A neuropsychological st
udy of binge eating and obesity Appetite, 54, 208–213.

Davis, C. L. R., Muglia, P., Bewell, C., & Kennedy, J. (2004). Decision-making deficits and overeating: A risk model for obesity. Obesity Research, 12(6), 929–35.

Davis, R. N., & Nolen-Hoeksema, S. (2000). Cognitive inflexibility among ruminators and nonruminators. Cognitive Therapy and Research, 24(6), 699–711.

Dingemans, A. E., Danner, U. N., Donker, J. M., Aardoom, J. J., van Meer, F. T., Obias, K., van Elburg, A. A., van Furth, E. F. (2014). Remediation therapy in patients with a severe or enduring eating disorder: a randomized controlled trial. Psychotherapy and Psychosomatics, 83(1), 29-36.

Disner, S. G., Beevers, C. G., Haigh, E. A. P., & Beck, A. T. (2011). Neural mechanisms of the cognitive model of depression. Nature Reviews Neuroscience, 12(8), 467–477.

Dixon, J. B., Dixon, M. E., & O'Brien, P. E. (2003). Depression in association with severe obesity: Changes with weight loss. Archives of Internal Medicine, 163(17), 2058–2065.

Donders, J., & Larsen, T. (2012). Clinical utility of the Tower of London—Drexel University, Second Edition (TOLDX) after adolescent traumatic brain injury. Developmental Neuropsychology, 37(4), 333-342. doi:10.1080/87565641.2011.646448

Duchesne, M., Mattos, P., Appolinário, J., de Freitas, S., Coutinho, G., Santos, C., & Coutinho,
W. (2010). Assessment of executive functions in obese individuals with binge eating disorder. Revista Brasileira de Psquiatria, 32(4), 381–388.

Eack, S. M., Hogarty, S. S., Greenwald, D. P., Litschge, M. Y., McKnight, S. A., Bangalore, S. S., … Cornelius, J. R. (2015). Cognitive Enhancement Therapy in substance misusing schizophrenia: results of an 18-month feasibility trial. Schizophrenia Research, 161(2- 3), 478-83.

Elgamal, S., Mckinnon, M. C., Ramakrishnan, K., Joffe, R. T., & Macqueen, G. (2007).

Successful computer-assisted cognitive remediation therapy in patients with unipolar depression: a proof of principle study. Psychological Medicine, 37(9), 1229-1238.

Elias, M. F., Elias, P. K., Sullivan, L. M., Wolf, P. A., & D'Agostino, R. B. (2003). Lower cognitive function in the presence of obesity and hypertension: The Framingham heart study. International Journal Of Obesity, 27(2), 260-268.

Fagundo, A. B., de la Torre, R., Jimenez-Murcia, S., Aguera, Z., Ganero, R., Tarrega, S., … Fernandez-Aranda, P. (2012). Executive Functions Profile in Extreme Eating/Weight Conditions: From Anorexia Nervosa to Obesity. PLoS One , 7(8).

Fairburn, C. G. (2008). Cognitive Behavior Therapy and Eating Disorders. New York: Guilford Press.

Faulconbridge, L. F., Wadden, T. A., Rubin, R. R., Wing, R. R., Walkup, M. P., Fabricatore, A. N., Coday, M., Van Dorsten, B., Mount, D. L., Ewing, L. J. and Look AHEAD Research Group (2012), One-Year Changes in Symptoms of Depression and Weight in Overweight/Obese Individuals With Type 2 Diabetes in the Look AHEAD Study.
Obesity, 20: 783–793. doi: 10.1038/oby.2011.315

Fontaine, K. R., & Barofsky, I. (2001). Obesity and quality of life. Obesity Reviews 2(4), 173– 182.

Franz, M. J., VanWormer, J. J., Crain, A. L., Boucher, J. L., Histon, T., Caplan, W., … Pronk,
N. (2007). Weight-Loss Outcomes: A Systematic Review and Meta-Analysis of Weight-Loss Clinical Trials with a Minimum 1-Year Follow-Up. Journal of the American Dietetic Association, 107(10) , 1755 – 1767.

Grant, D. A. (1951). Perceptual versus analytical responses to the number concept of a Weigl- type card sorting test. Journal of Experimental Psychology, 41(1), 23-29.

Grucza, R, A., Przybeck, T. R., & Cloninger, C. R. (2007). Prevalence and correlates of binge eating disorder in a community sample. Comprehensive Psychiatry, 48(2), 124-131.

Gunstad, J., Lhotsky, A., Wendell, C. R., Ferrucci, L., & Zonderman, A. B. (2010). Longitudinal examination of obesity and cognitive function: results from the Baltimore Longitudinal Study of Aging. Neuroepidemiology, 34(4), 222-229.

Hall, P. A. (2013). Temporal self-regulation theory. In M. D. Gellman and J. R. Turner (Eds.), Encyclopedia of Behavioral Medicine (pp. 1960-1963). New York, NY: Springer.

Hall P. A., Elias L. J., Crossley M. (2006). Neurocognitive influences on health behavior in a community sample. Health Psychol. 25, 778–782 10.1037/0278-6133.25.6.778

Harris, M. E. (1990). Wisconsin Card Sorting Test: Computer version, research edition. Odessa,
FL: Psychological Assessment Resources.

Heaton, R. K. (1981). A manual for the wisconsin card sorting test. Odessa, FL: Psychological Assessment Resources.

Henderson, K. E., & Brownell, K. D. (2004). The toxic environment and obesity: Contribution and cure. In J. K. Thompson (Ed), Handbook of Eating Disorders and Obesity (pp. 339- 348). New Jersey: John Wiley & Sons.

Henry, J.D., & Crawford, J. R. (2005). The 21-item version of the Depression Anxiety Stress Scales (DASS–21): Construct validity and normative data in a large non-clinical sample. British Journal of Clinical Psychology, 44, 227-239.

Houben, K., Nederkoorn, C., Jansen, A. (2014). Eating on impulse: the relation between overweight and food-specific inhibitory control. Obesity, 22(5): E6–E8.

Houben, K., & Jansen, A. (2011). Training inhibitory control: recipe for resisting sweet temptations. Appetite, 56(2), 345-9.

Houben K. (2011). Overcoming the urge to splurge: Influencing eating behavior by manipulating inhibitory control. Journal of Behavior Therapy and Experimental Psychiatry, 42, 384–388. [PubMed]

Houben, K., Wiers, R. W., & Jansen, A. (2011). Getting a grip on drinking behavior: training working memory to reduce alcohol abuse. Psychological Science, 22(7), 968–975.

James, L. C., & Linton, J. C. (2009). Handbook of obesity intervention for the lifespan. New York, NY, US: Springer Science + Business Media.

Kolotkin, R. L., Norquist, J. M., Crosby, R. D., Suryawanshi, S., Teixeira, P. J., Heymsfield, S. B., … Nguyen, A. M. (2009). One-year health-related quality of life outcomes in weight loss trial participants: comparison of three measures. Health and Quality of Life Outcomes, 7, 53.

Kolotkin, R. L, Meter, K., & Williams, G. R. (2001). Quality of life and obesity. Obesity Reviews 2(4): 219–229.

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel, D. (2012). Neuropsychological assessment (5th ed.). New York, NY, US: Oxford University Press.

Littell, R. C., Milliken, G. A., Stroup W. W., Wolfinger, R. D., Schabenberger, O. (2006). SAS for Mixed Models, 2nd edition. Cary, NC: SAS Institute.

Luchsinger, J. A. (2012). Type 2 diabetes and cognitive impairment: linking mechanisms. *Journal of Alzheimer's Disease*, *30*(0), S185–S198. http://doi.org/10.3233/JAD-2012-111433.

Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. H., & Zitman,
F. (2010). Overweight, obesity and depression: a systematic meta-analysis of longitudinal studies. Archives Of General Psychiatry, 67(3), 220-229.

Manwaring, J. L., Green, L., Myerson, J., Strube, M. J., Wilfley, & D. E. (2011). Discounting of various types of rewards by women with and without binge eating disorder: evidence for general rather than specific differences. The Psychological Record, 61(4), 561–582.

Marazziti, D., Consoli, G., Picchetti, M., Carlini, M., & Faravelli, L. (2010). Cognitive impairment in major depression. European Journal of Pharmacology, 626 (1), 83–86.

Masheb, R.M., & Grilo, C.M. (2002). On the relation of flexible and rigid control of eating to body mass index and overeating in patients with binge eating disorder. Int. J. Eat. Disord., 31, 82–91

Miyake, A., Freidman, N.P., Emerson, M.J., Wizki, A.H., Howerter, A., & Wager, T.D. (2000).
The unity and diversity of executive functions and their contributions to complex 'frontal lobe' tasks: A latent variable analysis. Cognit. Psychology, 41, 49–100.

Mobbs, O., Crepin, C., Thiery, C., Golay, A., & Van der Linden, M. (2010). Obesity and the four facets of impulsivity. Patient Education and Counselling, 79 (3), 372-377.

Mond, J. M., Hay, P. J., Rodgers, B., Owen, C., & Beumont, P. J. V. (2004). Validity of the Eating Disorder Examination Questionnaire (EDE-Q) in screening for eating disorders in community samples. Behaviour Research and Therapy, 42(5), 551-567.

Morris, N., & Jones, D. M. (1990). Memory updating in working memory: The role of

the central executive. British Journal Of Psychology, 81(2), 111-121. doi:10.1111/j.2044- 8295.1990.tb02349.x

Palmeira, A. L., Markland, D. A, Silva, M. N., Branco, T. L., Martins, S. C., Minderico, C. S.,
… Teixeira, P. J. (2009). Reciprocal effects among changes in weight, body image, and other psychological factors during behavioral obesity treatment: a mediation
analysis. International Journal of Behavioral Nutrition and Physical Activity, 6.

Perpiñá, C., Segura, M. & Sánchez-Reales, S. (2016). Cognitive flexibility and decision-making in eating disorders and obesity. Eat Weight Disord, . Eat Weight Disord. 2016 Oct 15. [Epub ahead of print] doi:10.1007/s40519-016-0331-3.

Péron, J., El Tamer, S., & Grandjean, D., Leray, E., Travers, D., Drapier, D., … Millet, B. (2011). Major depressive disorder skews the recognition of emotional prosody, Progress in Neuro-Psychopharmacology and Biological Psychiatry, 35(4), 987–996.

Pignatti, R., Bertella, L., Albani, G., Mauro, A., Molinari, E., & Semenza, C. (2006). Decision- making in obesity: A study using the Gambling Task. Eating And Weight Disorders, 11(3), 126-132. doi:10.1007/BF03327557

Price, M., Lee, M., & Higgs, S. (2016). Food-specific response inhibition, dietary restraint and snack intake in lean and overweight/obese adults: a moderated-mediation model. International Journal of Obesity (2005), 40(5), 877–882. http://doi.org/10.1038/ijo.2015.235

Rahmouni, K., Correia, M. L., Haynes, W. G., & Mark, A. L. (2005). Obesity-associated hypertension: new insights into mechanisms. Hypertension, 45(1), 9–14.

Raman, J., Hay, P., & Smith, E. (2014). Manualised Cognitive Remediation Therapy for adult obesity: study protocol for a randomised controlled trial. *Trials*, *15*(1), 426. doi:10.1186/1745-6215-15-426

Raman, J., Smith, E., & Hay, P. (2013). The Clinical Obesity Maintenance Model: An Integration of Psychological Constructs including Mood, Emotional Regulation, Disordered Overeating, Habitual Cluster Behaviours, Health Literacy and Cognitive Function. Journal of Obesity,. 2013, Article ID 240128, 9 pages, doi:10.1155/2013/240128

Reitz, C., Tang, M.-X., Manly, J., Mayeux, R., & Luchsinger, J. A. (2007). Hypertension and the Risk of Mild Cognitive Impairment. *Archives of Neurology*, *64*(12), 1734–1740. http://doi.org/10.1001/archneur.64.12.1734

Renn, B. N., Feliciano, L., & Segal, D. L. (2011). The bidirectional relationship of depression and diabetes: a systematic review. Clinical Psychological Review, 31(8), 1239-1246.

Robbins, T. W. (1998). Dissociating executive functions of the prefrontal cortex. In A. C. Roberts, T. W. Robbins, & L. Weiskrantz (Eds.), The prefrontal cortex. Executive and cognitive function (pp. 117–131). Oxford: Oxford University Press.

Roberts, M., Tchanturia, K., Stahl, D., Southgate, L., & Treasure, J. (2007). A systematic review and meta-analysis of set shifting ability in eating disorders. Psychol. Med. 37(8), 1075–1081.

Roberts, M., Dermetriou, L., & Tchanturia, K. (2007) Neuropsychological profile in the overweight population: An exploratory study of set-shifting and detail focused processing styles. Therapy, 4(6), 1-4.

Rupp, C. I., Kemmler, G., Kurz, M., Hinterhuber, H., & Fleischhacker, W. W. (2012). Cognitive remediation therapy during treatment for alcohol dependence. Journal Of Studies On Alcohol And Drugs, 73(4), 625-634.

Sapolsky, R. M. (1999). Glucocorticoids, stress, and their adverse neurological effects: relevance to aging. Experimental Gerontology, 34(6), 721–732.

Saykin, A. J., de Ruiter, M. B., McDonald, B. C., Deprez, S., & Silverman, D. H. S. (2013).
Neuroimaging Biomarkers and Cognitive Function in Non-CNS Cancer and Its Treatment: Current Status and Recommendations for Future Research. *Brain Imaging and Behavior*, *7*(4), 363–373. http://doi.org/10.1007/s11682-013-9283-7

Sellbom, K.S,, & Gunstad, J. (2012). Cognitive function and decline in obesity. J. Alzheimers Dis, 30(2), 89-S95.

Shaw, K.A., O'Rourke, P., Del Mar, C., & Kenardy, J. (2005). Psychological interventions for overweight or obesity. Cochrane Database of Systematic Reviews, 2, Art. No: CD003818. DOI: 10.1002/14651858.CD003818.pub2.

Siervo, M., Arnold, R., Wells, J. C. K., Tagliabue, A., Colantuoni, A., Albanese, E., Brayne, C. and Stephan, B. C. M. (2011), Intentional weight loss in overweight and obese individuals and cognitive function: a systematic review and meta-analysis. Obesity Reviews, 12: 968–983. doi: 10.1111/j.1467-789X.2011.00903.x

Simon, G. E., Rohde, P., Ludman, E. J., Jeffery, R. W., Operskalski, B. H., & Arterburn, D. (2010). Association between change in depression and change in weight among women enrolled in weight loss treatment. General Hospital Psychiatry, 32(6), 583–589.

Smith, E., Hay, P., & Raman, J. (2015). Cognitive remediation therapy for obesity. In K. Tchanturia, K. Tchanturia (Eds.) , Cognitive remediation therapy (CRT) for eating and weight disorders (pp. 176-191). New York, NY, US: Routledge/Taylor & Francis Group.

Smith, E., Hay, P., Campbell, L., & Trollor, J. (2011). A review of the relationship between obesity and cognition across the lifespan: implications for novel approaches to prevention and treatment. Obesity Reviews, 12(9), 740-755, 814–831.

Smith, P. J., Blumenthal, J. A., Babyak, M. A., Craighead, L., Welsh-Bohmer, K. A., Browndyke, J. N., … Sherwood, A. (2010). Effects of the Dietary Approaches to Stop Hypertension Diet, Exercise, and Caloric Restriction on Neurocognition in Overweight Adults With High Blood Pressure. *Hypertension*,*55*(6), 1331–1338. http://doi.org/10.1161/HYPERTENSIONAHA.109.146795

Stanek, K. M., & Gunstad, J. (2013). Can bariatric surgery reduce risk of Alzheimer's disease?
Progress in Neuro-Psychopharmacology & Biological Psychiatry, 47, 135–139.

Svaldi, J., Naumann, E., Trentowska, M., & Schmitz, F. (2014). General and food-specific inhibitory deficits in binge eating disorder. International Journal of Eating Disorders, 47(5), 534–542. Svaldi, J., Griepenstroh, J., Tuschen-Caffier, B., Ehring, T. (2012). Emotion regulation deficits in eating disorders: a marker of eating pathology or general psychopathology? Psychiatry Research, 197(1-2), 103–111.

Svaldi, J., Brand, M., & Tuschen-Caffier, B. (2010). Decision-making impairments in women with binge eating disorder. Appetite, 54(1), 84–92.

Tchanturia, K., Westwood, H., & Davies, H. (2015). Cognitive remediation therapy for anorexia nervosa: How do we know it works?. In K. Tchanturia, K. Tchanturia (Eds.), *Cognitive*
remediation therapy (CRT) for eating and weight disorders (pp. 192-206). New York, NY, US: Routledge/Taylor & Francis Group.

Tchanturia, K., Lounes, N., Holttum, S. (2014). Cognitive Remediation in Anorexia Nervosa and Related Conditions: A Systematic Review. European Eating

Disorders Review, 22(6), 454-462.
Tchanturia, K., Davies, H., Lopez, C., Schmidt, U., Treasure, J., & Wykes, T. (2008) Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: A pilot case series Psychological Medicine 38(9):1371-1373
Tchanturia, K., Liao, T., Uher, R., Lawrence, N., Treasure, J., & Campbell, I. (2007) An investigation of decision making in people with anorexia nervosa using Iowa Gambling task and skin conductance measurements The Journal of International Neuropsychological Society. 13, 635-641.
Tchanturia, K., Anderluh, M. B., Morris, R. G., Rabe-Hesketh, S., Collier, D. A., Sanchez, P., & Treasure, J. L. (2004). Cognitive flexibility in anorexia nervosa and bulimia nervosa.
Journal Of The International Neuropsychological Society, 10(4), 513-520. doi:10.1017/S1355617704104086
Texeira, P. J., Going, S. B., Houtkooper, L. B., Cussler, E. C., Metcalfe, L. L., Blew, R. M., … Lohman, T. G. (2004). Pretreatment predictors of attrition and successful weight management in women. International Journal of Obesity and Related Metabolic Disorders. 28(9), 1124-1133.
Teunissen, C.E., van Boxtel, M.P.J., Bosma, H., Bosmans, E, Delanghe, J., De Bruijn, C., Wauters, A., Maes, M., Jolles, J., Steinbusch, H.W.M., & de Vente, J. (2003).
Inflammation markers in relation to cognition in a healthy aging population. Journal of Neuroimmunology. 134 (1–2), 142-150.
Uekermann, J., Channon, S., Lehmkämper, C., Abdel-Hamid, M., Vollmoeller, W., & Daum, I. (2008). Executive function, mentalizing and humor in major depression. Journal of the International Neuropsychological Society, 14(1), 55–62.
Veling, H., Aarts, H., Stroebe, W. (2011). Using stop signals to reduce impulsive choices for palatable unhealthy foods. British Journal of Health Psychology, 18(2), 354-368.
Verbeken, S., Braet, C., Goossens, L., & van der Oord, S. (2013). Executive function training with game elements for obese children: a novel treatment to enhance self-regulatory abilities for weight-control. Behaviour Research and Therapy, 51(6), 290–299.
Vocks, S., Tuschen-Caffier, B., Pietrowsky, R., Rustenbach, S. J., Kersting, A., & Herpertz, S. (2010). Meta-analysis of the effectiveness of psychological and pharmacological treatments for binge eating disorder. *International Journal Of Eating Disorders, 43*(3), 205-217.
Voon, V. (2015). Cognitive biases in binge eating disorder: the hijacking of decision making. CNS Spectrums, 20(6), 566–573.
http://doi.org/10.1017/S1092852915000681
Ward, H., Shum, D., McKinlay, L., Baker, S., & Wallace, G. (2007). Prospective memory and pediatric traumatic brain injury: Effects of cognitive demand. Child Neuropsychology, 13(3), 219-239. doi:10.1080/09297040600910003
Ware, J. Jr., Kosinski, M., Keller, S. D. (1996). A 12 Item Short Form health survey: construction of scales and preliminary tests of reliability and validity. Medical Care, 34(4), 220-233.
Watkins, E., & Teasdale, J. D. (2001). Rumination and overgeneral memory in depression: effects of self-focus and analytic thinking. Journal of Abnormal Psychology, 110(2), 3 53–357.
Wilbertrz, G., Tebartz van E. L., Delgado, M. R., Maier, S., Feige, B., Philipsen, A., Blechert, J. (2012). Orbitofrontal reward sensitivity and impulsivity in adult attention deficit hyperactivity disorder. Neuroimage**,** 60(1), 353-361**.**

Williamson, D. A., Rejeski, J., Lang, W., Van Dorsten, B., Fabricatore, A. N., & the Look AHEAD Research Group K. (2009). Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. Archives of Internal Medicine, 169(2), 163-171.

Willis S. L., Tennstedt S. L., Marsiske M., Ball K., Elias J., Koepke K. M., Morris, J. N., … ACTIVE Study Group. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. Journal of the American Medical Association, 296(23), 2805–2814.

Wing, R. R., & Hill, J. O. (2001). Successful weight loss maintenance. Annual Review of Nutrition, 21, 323-341.

Wu, M., Brockmeyer, T., Hartmann, M., Skunde, M., Herzog, W., Friederich, H.C. (2014). Set- shifting ability across the spectrum of eating disorders and in overweight and obesity: a systematic review and meta-analysis. Psychological Medicine, 44 (16), 3365-3385.
DOI 10.1017/S0033291714000294

Wu, M., Giel, K. E., Skunde, M., Schag, K., Rudofsky, G., de Zwaan, M., …Friederich, H. C. (2013). Inhibitory control and decision making under risk in bulimia nervosa and binge- eating disorder. International Journal of Eating Disorders, 46 (7), 721–728.

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: Methodology and effect sizes. The American Journal Of Psychiatry, 168(5), 472-485.
doi:10.1176/appi.ajp.2010.10060855

Ylikoski, R., Ylikoski, A., Raininko, R., Keskivaara, P., Sulkava, R., Tilvis, R., Erkinjuntti, T. (2000). Cardiovascular diseases, health status, brain imaging findings and neuropsychological functioning in neurologically healthy elderly individuals. Archives of Gerontology and Geriatrics, 30(2), 115–

Appendix A

Variance of Random Intercept and Residual

Outcome	Variance	Estimate	SE	P-Value
WCST	Intercept	9.23	2.32	<.0001
	Residual	11.67	1.44	<.0001
TMT	Intercept	134.09	51.29	.005
	Residual	442.00	53.87	<.0001
Weight change in percentage	Intercept	0.00	.	.
	Residual	12.33	1.20	<.0001
BMI	Intercept	56.59	9.21	<.0001
	Residual	2.36	0.29	<.0001
Binge eating frequency	Intercept	48.04	10.41	<.0001
	Residual	34.27	4.49	<.0001
Depression	Intercept	62.53	14.61	<.0001
	Residual	60.44	7.51	<.0001
Mental quality of life	Intercept	37.03	11.37	<.001
	Residual	67.01	8.99	<.0001

This table shows the variance estimates and associated p-values of random intercept and residual for each model. Note that, except for weight change in percentage, the variances of all the random intercepts considered here are comparable to corresponding residual variances, and statistically significant. This justifies the introduction of random intercept in our model. Variance of random intercept for the outcome weight change in percentage, is estimated as zero as all the values of weight change in percentage at baseline is 0 by definition and hence becomes a degenerate variables with variance zero.

Appendix B

Figures 1-5 show trends of significant outcomes by group, taking linear regression for each subject's measurement as well for all the subjects at once (in red). In these plot the time is plotted as a continuum though the measurements are taken at baseline, post intervention and at 3 month follow up for significant outcome variables. These figures again suggest better outcomes for the treatment group.

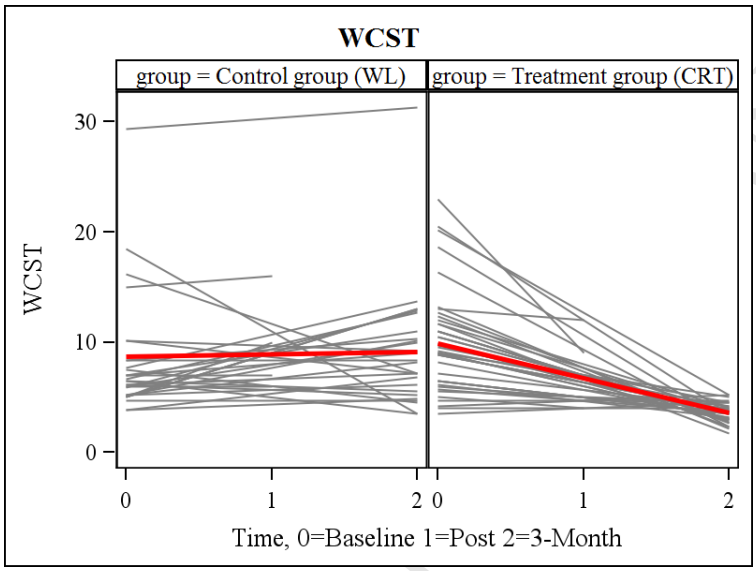


Figure 1.
Trend in WCST Preservative Errors across Baseline, Post Intervention and 3 month follow up

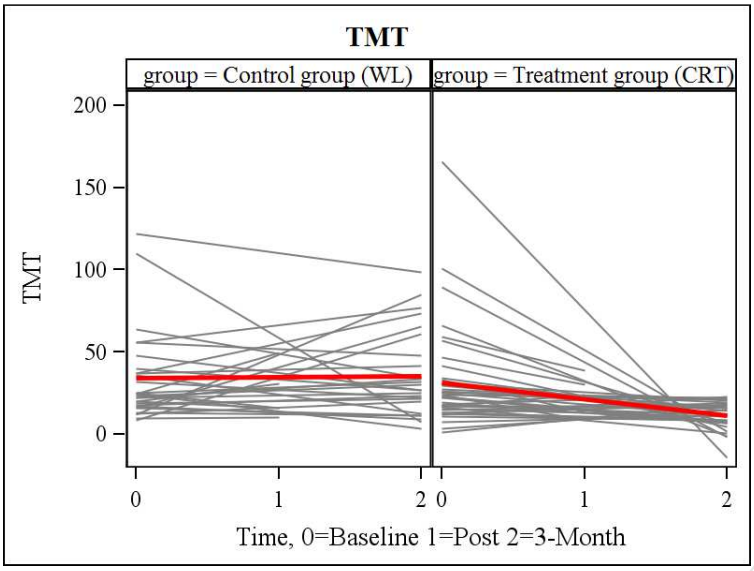


Figure 2
Trend in TMT Derived Score across Baseline, Post Intervention and 3 month follow up

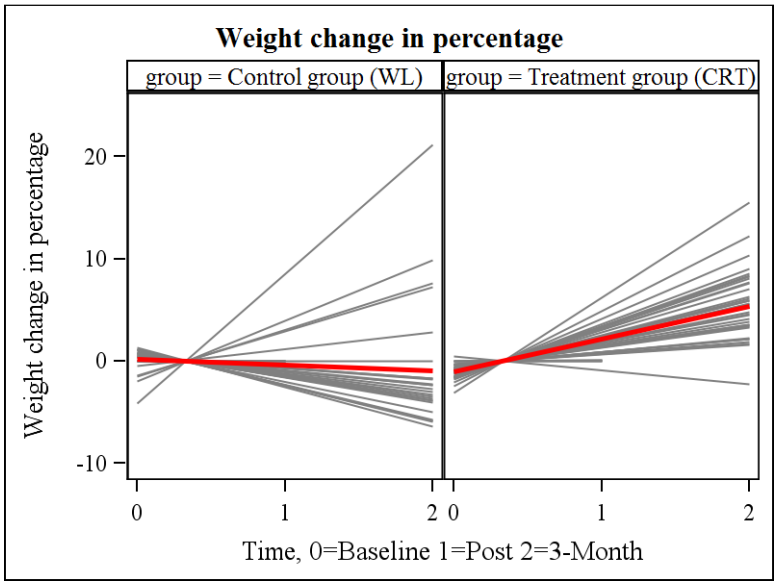


Figure 3
Trend in Weight change in % across Baseline, Post Intervention and 3 month follow up

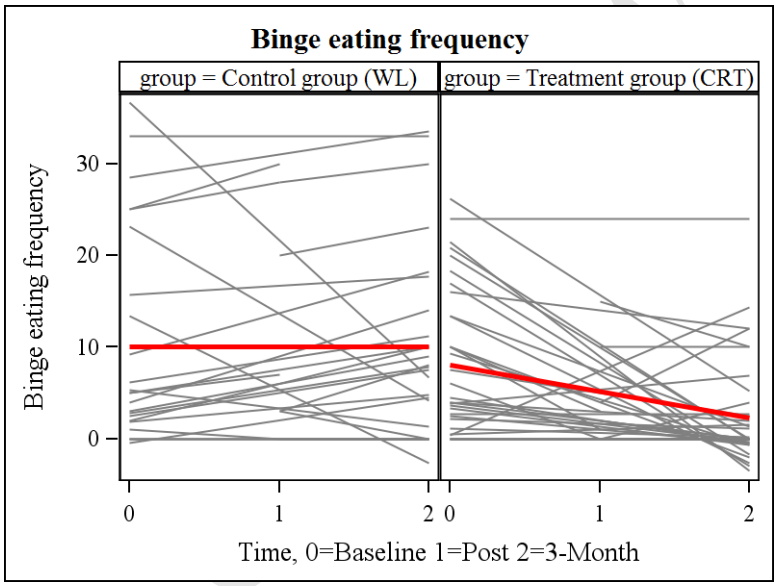


Figure 4
Trend in Binge eating frequency across Baseline, Post Intervention and 3 month follow up

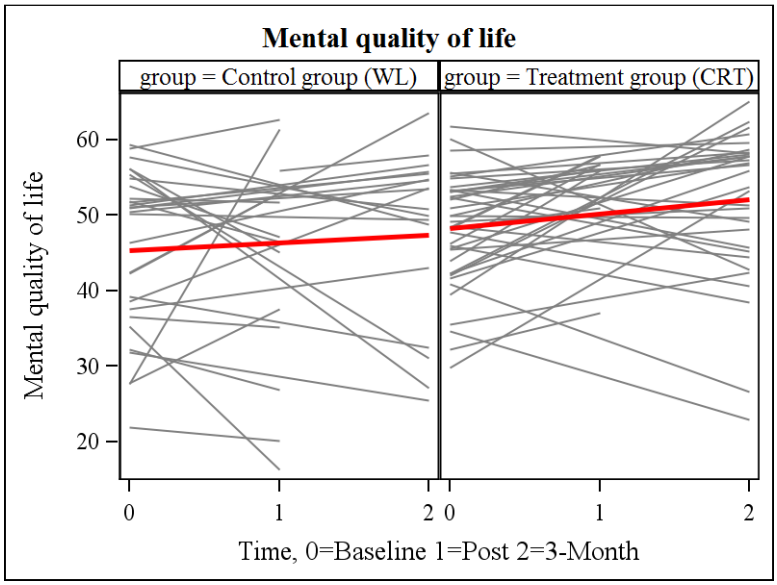


Figure 5
Trend in Mental quality of life across Baseline, Post Intervention and 3 month follow up